New Respiratory Syncytial Virus (RSV) Vaccines for Adults: General Information and Clinical Guidance

Current Issues in Immunization Webinar, August 30th, 2023

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In June 2023, CDC’s Advisory Committee on Immunization Practices (ACIP) recommended the first two RSV vaccines for older adults.

- **RSVPreF3** *(Arexvy, GSK)* is a 1-dose adjuvanted (AS01\_E) recombinant prefusion F protein (preF) vaccine.

- **RSVpreF** *(Abrysvo, Pfizer)* is a 1-dose recombinant preF vaccine.

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
ACIP recommendation for the use of RSV vaccines in older adults:

Adults aged 60 years and older may receive a single dose of RSV vaccine, using shared clinical decision-making.

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
Respiratory Syncytial Virus (RSV) in Adults
About Respiratory Syncytial Virus (RSV)

- **Common respiratory virus**
- Causes mild, cold-like symptoms
- Seasonal epidemics
- Spread through respiratory droplets, direct contact, fomites

[https://www.cdc.gov/rsv/index.html](https://www.cdc.gov/rsv/index.html)
About Respiratory Syncytial Virus (RSV)

Common respiratory virus

Causes mild, cold-like symptoms

Seasonal epidemics

Spread through respiratory droplets, direct contact, fomites

https://www.cdc.gov/rsv/index.html
Changes in seasonality of RSV transmission following SARS-CoV2 introduction—NREVSS\textsuperscript{1}, 2017–2023

Abbreviation: PCR = polymerase chain reaction; RSV = respiratory syncytial virus. 

\textsuperscript{1} https://www.cdc.gov/mmwr/volumes/72/wr/mm7214a1.htm

* 3-week centered moving averages of percentage of RSV-positive PCR results nationwide. The black dotted line represents the threshold for a seasonal epidemic (3% RSV-positive laboratory PCR results).
Changes in seasonality of RSV transmission following SARS-CoV2 introduction—NREVSS\(^1\), 2017–2023

Abbreviation: PCR = polymerase chain reaction; RSV = respiratory syncytial virus.

1. https://www.cdc.gov/mmwr/volumes/72/wr/mm7214a1.htm

* 3-week centered moving averages of percentage of RSV-positive PCR results nationwide. The black dotted line represents the threshold for a seasonal epidemic (3% RSV-positive laboratory PCR results).
Clinical Presentation in Adults

- Usually **mild or no symptoms**
- Older adults are at **increased risk** for becoming **seriously ill**
- This includes:
  - Lower respiratory tract infection
  - Exacerbation of existing conditions

https://www.cdc.gov/rsv/clinical/index.html
Annual RSV Burden Among Adults Ages 65 Years and Older

- **900,000–1,400,000** medical encounters
- **60,000–160,000** hospitalizations
- **6,000–10,000** deaths

[Link to source](https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-02/slides-02-23/RSV-Adults-04-Melgar-508.pdf)
Chronic Underlying Medical Conditions Associated with Increased Risk of Severe RSV Disease

- Lung disease
- Cardiovascular disease
- Moderate or severe immune compromise
- Diabetes Mellitus
- Neurologic or neuromuscular conditions
- Kidney disorders
- Liver disorders
- Hematologic disorders

Other conditions that might increase the risk for severe disease

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
### Underlying medical conditions among adults ≥18 years hospitalized with lab-confirmed RSV: RSV-NET 2014–2018

<table>
<thead>
<tr>
<th>Major underlying condition categories</th>
<th>N=4,970</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease</td>
<td>2833</td>
<td>57.0</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>2486</td>
<td>50.0</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1692</td>
<td>34.0</td>
</tr>
<tr>
<td>Renal disease</td>
<td>1378</td>
<td>27.7</td>
</tr>
<tr>
<td>Immunocompromised condition</td>
<td>1126</td>
<td>22.7</td>
</tr>
<tr>
<td>Neurologic disorder</td>
<td>1041</td>
<td>21.0</td>
</tr>
<tr>
<td>Chronic metabolic disease (except diabetes)</td>
<td>934</td>
<td>18.8</td>
</tr>
<tr>
<td>Liver disease</td>
<td>332</td>
<td>6.7</td>
</tr>
<tr>
<td>Blood disorders/ hemoglobinopathy</td>
<td>132</td>
<td>2.7</td>
</tr>
<tr>
<td>Other disease or condition</td>
<td>429</td>
<td>8.7</td>
</tr>
</tbody>
</table>

94% of hospitalized adults have underlying medical conditions:

- 46%: 1–2 conditions
- 48%: ≥3 conditions

Other Factors Associated with Increased Risk of Severe RSV Disease

- Residence in a nursing home or other long-term care facility (LTCF)
- Frailty
- Advanced age

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
Other Factors Associated with Increased Risk of Severe RSV Disease

- Residence in a nursing home or other long-term care facility (LTCF)
- Frailty
- Advanced age

- Residents may have many other risk factors
- RSV can cause serious outbreaks in LTCFs

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
**Long-term care facility (LTCF) residents vulnerable to outbreaks and serious illness**

- Frequent cause of symptomatic illnesses in LTCF residents
- High attack rate in outbreak settings
  - 13.5% over 1 month
- Study of Medicare data estimated RSV-attributable hospitalizations over 6 years
  - 2,909,106 LTCF residents ≥65 years
  - 6,196 cardiorespiratory hospitalizations

<table>
<thead>
<tr>
<th>Attributable cost</th>
<th>$51,503,105 ($38,899,971 – $64,106,240)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay (LOS)</td>
<td>5.3 days (SE 4.6)</td>
</tr>
<tr>
<td>Attributable LOS</td>
<td>32,008 days (95% CI 24,267 – 39,749)</td>
</tr>
</tbody>
</table>

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- Frailty
- Advanced age

RSV incidence increases with **advancing age.**

[Reference](https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm)
RSV-NET estimated annual hospitalizations per 100,000 adults: 2016–2017 to 2019–2020

CDC RSV-NET unpublished data. Estimates are adjusted for under-testing and incomplete test sensitivity. [https://www.cdc.gov/rsv/research/rsv-net/index.html](https://www.cdc.gov/rsv/research/rsv-net/index.html)
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RSV Vaccines

Efficacy and safety
Vaccine Efficacy (VE)

- Vaccines had **similar** and **high** VE against RSV-associated lower respiratory tract disease.

- Case definitions for primary outcomes were **not aligned** across trials.
Vaccine Efficacy (VE): GSK

- One primary outcome: RSV lower respiratory tract disease (LRTD)
  - At least **two** lower respiratory **symptoms** or **signs**, including at least one **sign**, OR
  - At least **three** lower respiratory **symptoms**

**Symptoms**
- Sputum
- Cough
- Dyspnea

**Signs**
- Wheezing
- Crackles/rhonchi
- Tachypnea
- Hypoxemia
- Oxygen supplementation

[https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm](https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm)
Vaccine Efficacy (VE): GSK

- Randomized, double-blind, placebo-controlled phase 3 clinical trial
  - 17 countries
  - 24,973 participants
- VE against RSV-associated lower respiratory tract disease (LRTD):

  Season 1: 82.6%
  Season 2: 56.1%
  Combined Season 1 & 2 (Interim): 74.5%

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
Vaccine Efficacy (VE): Pfizer

- Two primary outcomes
  - RSV lower respiratory tract illness (LRTI) with at least two lower respiratory signs/symptoms
  - RSV LRTI with at least three lower respiratory signs/symptoms

**Signs/symptoms**

- Sputum
- Cough
- Shortness of breath
- Wheezing
- Tachypnea

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
Vaccine Efficacy (VE): Pfizer

- Randomized, double-blinded, placebo-controlled phase 3 clinical trial
  - 7 countries
  - 36,862 participants
- VE against RSV-associated lower respiratory tract disease (LRTD)*:

  - Season 1: 88.9%
  - Season 2 (Interim): 78.6%
  - Combined Season 1 & 2 (Interim): 84.4%

*Based on trial efficacy against RSV LRTI with at least three lower respiratory symptoms

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
Pfizer’s RSVpreF and GSK’s adjuvanted RSVPreF3 vaccines both have demonstrated significant efficacy against lower respiratory tract illness caused by RSV among older adults over at least two seasons

– Trials were underpowered to show efficacy in the oldest adults and in adults who are frail
– Trials were underpowered to show efficacy against RSV hospitalization
  • Efficacy against symptomatic illness may indicate efficacy against more severe disease

RSV vaccination has the potential to prevent considerable morbidity from RSV disease among older adults, particularly in those with chronic medical conditions and those who are frail (e.g., long-term care facility residents)

Vaccine Safety

- Generally well-tolerated with an acceptable safety profile

- Most common side effects are similar to those of other vaccines

Pain at injection site  Fatigue  Headache  Muscle pain  Joint pain

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
Vaccine Safety

- Six cases of inflammatory neurologic events reported in clinical trials.

- It is unknown at this time whether these events occurred by chance, or whether RSV vaccination increases the risk of these events.

- Imbalance in the small number of atrial fibrillation events; more cases among vaccine recipients, compared with placebo recipients.

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
Vaccine Safety

- CDC will **monitor adverse events** following RSV vaccination through VAERS and the Vaccine Safety Datalink.

- Per FDA requirements, both manufacturers will **conduct further studies**.

- Report any adverse event after RSV vaccination to the **Vaccine Adverse Event Reporting System**.

[Links]
- [CDC MMWR](https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm)
- [VAERS](https://vaers.hhs.gov/index.html)
Recommendations and Clinical Considerations
ACIP and CDC recommend that adults ages 60 years and older may receive a **single dose** of RSV vaccine using **shared clinical decision making**.

[https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm](https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm)
Shared clinical decision-making

- There is no **default decision** to vaccinate.
- Recommendations are **individually based** and informed by a decision process between the **health care provider and patient**.

**Best available evidence**

**Patients’ risk for disease, characteristics, values, preferences**

**Clinical discretion**

**Characteristics of the vaccine**

[https://www.cdc.gov/vaccines/acip/acip-scdm-faqs.html](https://www.cdc.gov/vaccines/acip/acip-scdm-faqs.html)
Chronic Underlying Medical Conditions Associated with Increased Risk of Severe RSV Disease

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Other conditions that might increase the risk for severe disease

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
Chronic Underlying Medical Conditions Associated with Increased Risk of Severe RSV Disease

- Many possible conditions
- Determining degree of immune compromise is at the discretion of the treating provider. Consider:
  - Disease severity
  - Duration
  - Clinical stability
  - Complications
  - Comorbidities
  - Immune-suppressing treatment

- Lung disease
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- Moderate or severe immune compromise
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https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
Vaccination Timing: 2023-2024 Season

**Summer:**
Offer RSV vaccination as early as vaccine is available

[https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm](https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm)
Vaccination Timing: 2023-2024 Season

**Summer:**
Offer RSV vaccination as early as vaccine is available

Continue to offer vaccination throughout the RSV season to eligible adults who remain unvaccinated

[https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm](https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm)
Data on immunogenicity of coadministration of RSV vaccines with other vaccines

• There are currently limited data available on immunogenicity of coadministration of RSV vaccines and other vaccines.

• In general, coadministration of RSV and seasonal influenza vaccines met non-inferiority criteria for immunogenicity.*

• However, RSV and influenza antibody titers were generally somewhat lower with coadministration; the clinical significance of this is unknown.

• Additional studies on immunogenicity of coadministration of RSV with other adult vaccines are in process.

* Pre-specified non-inferiority criteria for immune responses were met across trials, with the exception of the FluA/Darwin H3N2 strain after simultaneous administration of RSVPreF3 vaccine (Arexvy by GSK) and adjuvanted quadrivalent inactivated influenza vaccine.

Coadministration

- Coadministration with all other adult vaccines is acceptable.

- If vaccines are NOT administered the same day, there is no required interval between vaccines.

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
Considerations for Coadministration

- Whether the patient is **up to date** with currently recommended vaccines
- Likelihood of **returning**
- Risk for acquiring **vaccine-preventable disease**
- Vaccine **reactogenicity** profiles
- Patient **preferences**

[https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm](https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm)
Coadministration Best Practices

- Prepare each injectable vaccine **using a separate syringe**.

- **Label** each syringe.

- Separate injection sites by **1 inch or more**, if possible.

- Administer vaccines that may be more likely to cause a local reaction in **different limbs**, if possible.

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
RSV Vaccines

Storage and handling
RSV Vaccines for Adults Ages 60 Years and Older

There is no preferential recommendation; give whichever vaccine is available.

https://www.fda.gov/media/167805/download
https://www.fda.gov/media/168889/download
Photo source: GSK and Pfizer, Inc.
GSK/Arexy: Storage and Handling

BEFORE Reconstitution

Store **refrigerated** between 2°C and 8°C (36°F and 46°F)

Do **NOT freeze**

Protect from **light**

https://www.fda.gov/media/167805/download
GSK/Arexvy: Storage and Handling

BEFORE Reconstitution
- Protect from light
- Do NOT freeze

AFTER Reconstitution
- Store refrigerated between 2°C and 8°C (36°F and 46°F)
- OR at room temperature [up to 25°C (77°F)]
- Do NOT freeze
- Protect from light
- Use within 4 hours

https://www.fda.gov/media/167805/download
Pfizer/Abrysvo: Storage and Handling

BEFORE Reconstitution

Store **refrigerated** between 2°C and 8°C (36°F and 46°F)

Do NOT freeze
Pfizer/Abrysvo: Storage and Handling

BEFORE Reconstitution

Store refrigerated between 2°C and 8°C (36°F and 46°F)
Do NOT freeze

AFTER Reconstitution

Store at room temperature [15°C to 30°C (59°F to 86°F)]
Do NOT refrigerate
Do NOT freeze
Use within 4 hours

https://www.fda.gov/media/167805/download
Best Practices with Beyond-Use Date (BUD)

Always read the package insert.

Label the vial with the BUD and your initials.

Check the expiration date or BUD before administering the vaccine.

Discard vials not used before the expiration date or within the BUD.

https://www.cdc.gov/vaccines/pubs/pinkbook/vac-storage.html
Summary
RSV can cause serious illness in older adults.
Underlying medical conditions and other factors are associated with increased risk of severe RSV.
Two RSV vaccines are licensed.
Adults ages 60 years and older may receive a single dose of RSV vaccine, using shared clinical decision-making.
Coadministration with RSV and other adult vaccines is acceptable.
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1-800-CDC-INFO (232-4636)

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